Ibuprofen
Newborn use only

2020

<table>
<tr><td>Alert</td><td>Pedea is currently the only registered product with Therapeutic Goods Administration (TGA) for closure of patent ductus arteriosus in preterm infants <34 weeks gestation.
Neoprofen is not currently registered with TGA. It is available for use via the Special Access Scheme (SAS).
Caldolor is registered for fever reduction and postoperative pain in adults.</td></tr>
<tr><td>Indication</td><td>Patent ductus arteriosus.</td></tr>
<tr><td>Action</td><td>Prostaglandin inhibitor. Prostaglandins are important in maintaining ductal patency in utero.</td></tr>
<tr><td>Drug type</td><td>Non-steroidal anti-inflammatory drug (NSAID).</td></tr>
<tr><td>Trade name</td><td>Intravenous: Pedea (ibuprofen sodium), Neoprofen (ibuprofen lysine). Caldolor (ibuprofen arginine),
Oral: FenPaed, Advil, Bugesic, Chemist's Own, Dimetapp, iProfen, Nurofen</td></tr>
<tr><td>Presentation</td><td>IV:
Pedea (ibuprofen sodium) 10 mg in 2 mL vial.
Neoprofen (ibuprofen lysine) 20 mg in 2 mL vial.
Caldolor (ibuprofen arginine) 800 mg in 8 mL vial.

Oral: 100 mg/5 mL suspension</td></tr>
<tr><td>Dose</td><td>IV/ORAL
<table>
<tr><td>Post-natal Age</td><td>Day 1</td><td>Day 2</td><td>Day 3</td></tr>
<tr><td>< 72 hours</td><td>10 mg/kg/dose</td><td>5 mg/kg/dose</td><td>5 mg/kg/dose</td></tr>
<tr><td>≥ 72 hours (higher dose)</td><td>20 mg/kg/dose</td><td>10 mg/kg/dose</td><td>10 mg/kg/dose</td></tr>
<tr><td>≥ 72 hours (lower dose)</td><td>10 mg/kg/dose</td><td>5 mg/kg/dose</td><td>5 mg/kg/dose</td></tr>
</table>
A full course of ibuprofen may not be necessary if ductal constriction or closure is demonstrated [1,2].
A repeat course of treatment may be considered depending on continuing haemodynamic significance of the ductus arteriosus and relative contraindications to treatment [3]. Data are insufficient to determine the efficacy of a 3rd course [4].</td></tr>
<tr><td>Dose adjustment
Therapeutic hypothermia
ECMO
Renal impairment
Hepatic impairment</td><td>
Not applicable
Not applicable
Current evidence is insufficient to suggest any specific dose adjustment.
Not applicable</td></tr>
<tr><td>Maximum dose</td><td>20 mg/kg</td></tr>
<tr><td>Total cumulative dose</td><td>20−40 mg/kg</td></tr>
<tr><td>Route</td><td>IV, oral</td></tr>
<tr><td>Preparation</td><td>Pedea (ibuprofen sodium)
Can be administered undiluted.
If dilution is required draw up 2 mL (10 mg of ibuprofen) and add 2 mL of sodium chloride 0.9% or glucose 5% to make a final volume of 4 mL with a concentration of 2.5 mg/mL.

Neoprofen (ibuprofen lysine)
Draw up 1 mL (10 mg of ibuprofen) and add 3 mL of sodium chloride 0.9% or glucose 5% to make a final volume of 4 mL with a concentration of 2.5 mg/mL.

Caldolor (ibuprofen arginine)
Draw up 0.5 mL (50 mg of ibuprofen) and add 19.5 mL of sodium chloride 0.9% or glucose 5% to make a final volume of 20 mL with a concentration of 2.5 mg/mL.</td></tr>
<tr><td>Administration</td><td><u>IV infusion:</u>
Pedea − over 15 minutes.
Neoprofen − over 15 minutes
Caldolor − over 30 minutes

Do not use chlorhexidine to disinfect the neck of the ampoule.[31]</td></tr>
</table>

	Oral – give via intra-gastric tube, preferably with milk feed to minimise risk of gastrointestinal irritation. If baby is not on enteral feeds or breast milk is not available, give dose via intra-gastric tube and flush with 0.5 mL water for injection.
Monitoring	Urine output, cardiovascular status, serum biochemistry, renal function and for signs of bleeding.
Contraindications	Serious infection, active bleeding, thrombocytopenia or coagulopathy, necrotising enterocolitis or intestinal perforation, significant renal dysfunction, ductal dependent congenital heart disease, pulmonary hypertension and significant jaundice as may displace bilirubin from albumin.
Precautions	IV – nil Oral- nil
Drug interactions	Diuretics – Ibuprofen may reduce the effect of diuretics; whilst the diuretic may increase the risk of nephrotoxicity of NSAIDs in dehydrated patients. Anticoagulants – ibuprofen may increase the effect of anticoagulants and enhance the risk of bleeding. Nitric oxide – as both medicinal products have an inhibitory effect on platelet function, their combination may in theory increase the risk of bleeding. Corticosteroids – ibuprofen may increase the risk of gastrointestinal bleeding. Other NSAIDs – the concomitant use of more than one NSAID may increase risk of adverse reactions. Aminoglycosides – since ibuprofen may decrease the clearance of aminoglycosides, their co-administration may increase the risk of nephrotoxicity and ototoxicity. Fluconazole - Metabolism of ibuprofen may be inhibited, increasing its concentration. Systemic corticosteroids - Intestinal perforation has been described in infants treated with early dexamethasone and indomethacin. Although not described with ibuprofen, caution is advised.
Adverse reactions	Prophylactic use of ibuprofen is associated increased risks for oliguria, increase in serum creatinine levels, and increased risk of gastrointestinal haemorrhage.[5]. [LOE I] Ibuprofen for treatment of a PDA was associated with increased oliguria and increased creatinine. [LOE I] Compared to treatment of a PDA with indomethacin, ibuprofen was associated with reduced NEC, reduced oliguria and was associated with lower creatinine levels 72 hours after initiation of treatment.[6].[LOE I] Compared to paracetamol (acetaminophen), ibuprofen was associated with a high rate of gastrointestinal bleeding, higher creatinine and bilirubin levels, and lower platelet counts and daily urine output. [7]. There have been reports of pulmonary hypertension with use of ibuprofen, [5, 6] although the rate may be similar to that reported for indomethacin.[8]. Ibuprofen may displace bilirubin from albumin at high concentrations in vitro (200 micromol/L), [9] although this does not appear to occur in vivo at the concentrations associated with recommended doses (up to 100 micromol/L). [10].
Compatibility	Fluids: Pedea, neoprofen, caldolor - Sodium chloride 0.9%, glucose 5%. NeoProfen only- sterile water for injection.[36] Y site: Pedea : Not tested. Y site: Neoprofen: Ceftazidime, epinephrine hydrochloride, furosemide, heparin sodium, insulin, phenobarbital sodium, potassium chloride, sodium bicarbonate Y site: Caldolor: Metoprolol tartrate
Incompatibility	Caldolor (ibuprofen arginine), Neoprofen (ibuprofen lysine) and Pedea (ibuprofen sodium) - regard all other IV solutions and drugs as incompatible.
Stability	Caldolor: Diluted solutions are stable for up to 24 hours at room temperature (20−25° C) and room lighting. Neoprofen and Pedea: Discard unused portion once opened.
Storage	IV − store unopened vials at room temperature (20−25°C). Oral liquid − store below 25°C.

Excipients	PEDEA - Each 1 ml of PEDEA contains the following inactive ingredients: trometamol (3.78 mg), sodium hydroxide (0.14 mg), sodium chloride (7.3 mg), hydrochloric acid and water for injections. The headspace within the ampoules is filled with nitrogen. Caldolor – Each 1 mL of Caldolor also contains 78 mg of arginine at a molar ratio of 0.92:1 arginine: ibuprofen. Hydrochloric acid is added for pH adjustment. Neoprofen - Each mL of NeoProfen contains 17.1 mg of ibuprofen lysine (equivalent to 10 mg of (±)-ibuprofen) in Water for Injection. The pH is adjusted to 7.0 with sodium hydroxide or hydrochloric acid. Fenpaed - contains glycerol, xanthan gum, maltitol, polysorbate 80, saccharin sodium, citric acid monohydrate, sodium methyl hydroxybenzoate, sodium propyl hydroxybenzoate, purified water and strawberry flavour.
Special comments	Nil
Evidence	Refer to full version
Practice points	Refer to full version.
References	Refer to full version.

VERSION/NUMBER	**DATE**
Original	4/11/2015
Revised **1.1** **1.2**	 23/06/2016 23/02/2017
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REVIEW (5 years)	30/01/2025

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